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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,347	10/17/2003	John Gregory Slatter	01411.US1	2299

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EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/688,347	SLATTER, JOHN GREGORY	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The Status of Claims:

Claims 1-11 are pending.

Claims 1-11 have been rejected.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating a mammal for asthma, chronic obstructive pulmonary disease, allergic rhinitis, and infectious rhinitis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the current invention commensurate in scope with the claim.

The specification falls short because data essential for treating a mammal for asthma, chronic obstructive pulmonary disease, allergic rhinitis, and infectious rhinitis is not described in the specification.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,

3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention in claim 11 is the method for treating a mammal for asthma, chronic obstructive pulmonary disease, allergic rhinitis, and infectious rhinitis by administering the effective amount of a quaternary ammonium compound of formula I.

The State of the Prior Art

The state of the prior art is that according to US Patent Nos. (6,262,115), (5,674,895), (5,840,754), and (5,912,268), the claimed compound I can be used for treating urinary incontinence, while there is no effect on other diseases.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the working of a smooth-muscle relaxant, such as formula I would result in only the specific site distal to the cholinergic receptor; this kind of treatment can not translated to all

the possible treatment of asthma, chronic obstructive pulmonary disease, allergic rhinitis, and infectious rhinitis in regards to their therapeutic effects.

Hence, in the absence of a showing of correlation between the diseases claimed as capable of treatment by the compounds of formula I, one of skill in the art is unable to fully predict possible results from the administration of the claimed compounds of formula I due to the unpredictability of the role of using the compounds of formula I, i.e. whether promotion or inhibition would be beneficial for the treatment of the diseases.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the compounds of formula I can treat asthma, chronic obstructive pulmonary disease, allergic rhinitis, and infectious rhinitis. However, the specification is silent and fails to provide guidance as to whether the diseases listed (pages 1-3) require the application of the compounds of formula I for treatment, i.e. the specification fails to provide a correlation between the diseases listed and how the compounds of formula I can be used to treat them. Also, there is no direction and guidance for

the application of the compounds of formula I for the treatment of the above diseases.

The presence or absence of working examples

There is only one working example for the treatment based on bronchodilatory effect. Furthermore, there are not other working examples for any other diseases listed in the specification. Also, the compounds which are discloses in the specification have no pharmacological data regarding the treatment of any other disease besides bronchodilatory effect using the compound of example I shown on page 9 and have no data on the possible treatment of the other symptoms of the diseases. Also, the specification fails to provide working examples as to how the listed diseases can be treated by the bronchodilatory effect alone, i.e. again, there is no correlation between the diseases listed and the bronchodilatory effect of the claimed compounds .

The breadth of the claims

The breadth of the claims is that the compounds of formula I can treat asthma, chronic obstructive pulmonary disease, allergic rhinitis, and infectious rhinitis by using the compounds of formula I , without regards as to the after-affect of the bronchodilatory effect on the stated diseases.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what listed diseases would be benefited by the use of the claimed compounds and would furthermore then have to

determine whether the claimed compounds would provide treatment of the diseases by the bronchodilatory effect alone.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of formula I for the treatment of those diseases by the bronchodilatory effect alone. As a result, necessitating one of skill to perform an exhaustive search for which diseases can be treated by the compounds of formula I in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

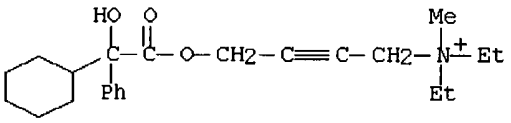
Claims 1-2 ,7 and 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated clearly by Guittard et al (U.S. 5,840,754) disclosed in the STN search.

Guittard et al discloses a derivative of oxybutynin in the following:

(oxybutynin compns. for management of incontinence)
RN 350229-43-5 CAPLUS
CN 2-Butyn-1-aminium, 4-[(cyclohexylhydroxyphenylacetyl)oxy]-N,N-diethyl-N-methyl-, nitrate (9CI) (CA INDEX NAME)

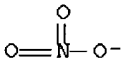
CM 1

CRN 350229-42-4
CMF C23 H34 N O3



CM 2

CRN 14797-55-8
CMF N O3



4-[(cyclohexylhydroxyphenylacetyl)oxy]-N,N-diethyl-N-methyl –2-butyn-1-aminium, nitrate (see col.10, lines 45-67). Furthermore, a therapeutic composition comprises an oxybutynin acceptable salt selected from hydrobromide, and hydrochloride (see col. 3 ,lines 36-40).This is identical with the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guittard et al (U.S. 5,840,754) disclosed in the STN search.

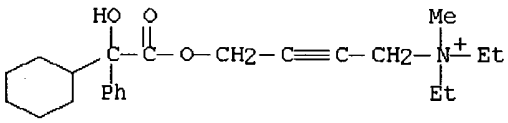
1. Determining the scope and contents of the prior art

Guittard et al discloses a derivative of oxybutynin in the following:

(oxybutynin compns. for management of incontinence)
RN 350229-43-5 CAPLUS
CN 2-Butyn-1-aminium, 4-[(cyclohexylhydroxyphenylacetyl)oxy]-N,N-diethyl-N-methyl-, nitrate (9CI) (CA INDEX NAME)

CM 1

CRN 350229-42-4
CMF C23 H34 N O3



CM 2

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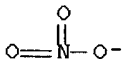
CMF N O3



, 4-[(cyclohexylhydroxyphenylacetyl)oxy]-N,N-diethyl-N-methyl –2-butyn-1-aminium, nitrate (see col.10, lines 45-67). Furthermore, a therapeutic composition comprises an oxybutynin acceptable salt selected from hydrobromide, and hydrochloride (see col. 3 ,lines 36-40).

2. Ascertaining the differences between the prior art and the claims at issue

However, the instant invention differs from the prior art in that the claimed anion of the pharmaceutically acceptable acid is iodide; the prior art does not disclose the formation of quaternary ammonium salt compound based on iodine.

3. Resolving the level of ordinary skill in the pertinent art

With respect to the claimed iodide anion of the pharmaceutically acceptable acid, Guittard et al does disclose the acceptable salt which can be selected from hydrobromide, and hydrochloride (see col. 3 ,lines 36-40). The iodide is belonged to the family of halogen containing Br, Cl, F, I and etc; they are similar among them with respect to their functionality. Therefore, it would have been obvious to the skilled artisan in the art to have motivated to select the iodide anion as an alternative to the pharmaceutically acceptable anions, such as bromide and chloride because the skilled artisan in the art would expect such a modification to be successful due to the similar functionality.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness

Guittard et al discloses 4-[(cyclohexylhydroxyphenylacetyl)oxy]-N,N-diethyl-N-methyl –2-butyn-1-aminium, nitrate (see col.10, lines 45-67). Furthermore, a therapeutic composition comprises an oxybutynin acceptable salt selected from hydrobromide, and hydrochloride (see col. 3 ,lines 36-40). Although the prior art does not disclose the formation of quaternary ammonium

salt compound based on iodine, the iodide is belonged to the family of halogen containing Br, Cl, F, I and etc; they are similar among them with respect to their functionality. Furthermore, it is obvious to form salts from the known acids. In re Williams, 89 USPQ 396 (CCPA 1951).

Therefore, if the skilled artisan in the art had desired to make the quaternary ammonium salt compound based on iodine, it would have been obvious to the skilled artisan in the art to have motivated to select the iodide anion as an alternative to the other pharmaceutically acceptable anions, such as bromide and chloride in the halogen family because the skilled artisan in the art would expect such a modification to be successful due to the similar functionality.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

***/ 9/9/07

BA K. TRINH
PRIMARY EXAMINER
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